REMARKS

The present application is refiled as an RCE.

Claims 1-6 have been cancelled without prejudice and new claims 7-9 are added. New claim 7 represents former claim 1 in combination with claims 2 and 3. New claims 8 and 9 correspond to former claims 4 and 5, respectively.

In the parent application, claims 1-6 are rejected under 35 USC 103 as unpatentable over U.S. Patent No. 5,725,874 or U.S. Patent No. 5,173,302. This ground of rejection of respectfully traversed as applied to the new claims in view of the following remarks.

The Examiner mentions that it is *prima facie* obvious to combine two compositions each of which is known to be useful for the same purpose, such as analgesics and anesthetics, both for relief of pain.

However, even if selecting arbitrarily any two compositions each of which is useful for relief of pain, the remarkable effect of the present invention cannot be expected.

The Applicant intends to establish the nonobviousness and patentability of the claimed invention by demonstrating that the claimed invention possesses an unexpected synergistic effect in comparison to administration of a random combination of anesthetic or analgesic taught in the prior art.

The instant specification contains Examples 1-6, Comparative Examples 1-4 and a Test Example.

Submitted herewith are supplemental Comparative Examples 5-8 and a Test Example 2.

Comparative Example 5

An external skin patch was prepared in the same production process employed in Example 1 except that 0.5 parts by weight of indomethacin was used instead of lidocaine. The total amount of the drug-containing base was fixed to 100 parts by weight by adjusting the amount of purified water. The amount of indomethacin was determined according to the amount used generally in Japan as an effective amount of the medicine.

Comparative Example 6

An external skin patch was prepared in the same production process employed in Example 1 except that 5 parts by weight of xylocaine was used instead of sodium diclofenac. The total amount of the drug-containing base was fixed to 100 parts by weight by adjusting the amount of purified water. The amount of xylocaine was determined according to the amount used generally in Japan as an effective amount of the medicine.

Comparative Example 7

An external skin patch was prepared in the same production process employed in Example 1 except that 0.1 parts by weight of betamethasone valerate, which was one of the steroidal anti-inflammatory agents cited in U.S. Patent No. 5,725,874, at column 2, lines 58-59, was used instead of lidocaine. The total amount of the drug-containing base was fixed to 100 parts by weight by adjusting the amount of purified water. The amount of betamethasone valerate was determined according to the amount used generally in Japan as an effective amount of the medicine.

Comparative Example 8

An external skin patch was prepared in the same production process employed in Example 1 except that 5.0 parts by weight of aspirin, which was one of the general analgetic agents cited in U.S. Patent No. 5,725,874, at column 3, line 13, was used instead of lidocaine. The total amount of the drug-containing based was fixed to 100 parts by weight by adjusting the amount of purified water. Since aspirin is rarely used as a drug for an external preparation, the amount of aspirin in this comparative example was determined in consideration of the circumstance of drug preparation.

Test Example 2

The external skin patches obtained in Example 1 and Comparative Examples 5-8 were administered randomly to 10 volunteers a group (total 50 persons) each having low back pain (i.e. plastered on the affected part) and an organoleptic examination was carried out. The duration of the administration was 12 hours a day and the test was carried out for 7 days. After the test, volunteers rated the results on a 1 to 4 scale ("complete remission", "effective", "unchanged" and "aggravation".) The results are given in Table 8.

Table 8

	Example 1	Comparative Example 5	Comparative Example 6	Comparative Example 7	Comparative Example 8
Complete Remission	7	2	1	1	1
Effective	3	5	5	4	5
Unchanged	0	2	4	5	4
Aggravation	0	1	0	0	0

As shown above, the amelioration ratio (effective or higher) of the external skin patches of Examples 1 and Comparative Examples 5 to 8 after 1 week was respectively 100% (10/10), 70% (7/10), 60% (6/10), 50% (5/10), and 60% (6/10), and the ratio of the Complete Remission was respectively 70% (7/10), 20% (2/10), 10% (1/10), 10% (1/10), and 10% (1/10).

This shows that the external skin path using the combination of the particular local anesthetic and the nonsteroidal antiphlogistic analgesic agent of the present invention (Example 1) achieves an unexpectedly superior pain relief effect compared to the external skin patches using any other combination of the compounds which are known to be useful for relief pain (Comparative Examples 5-8).

Thus, it is not obvious to the skilled artisan that using the specific combination of the local anesthetic and the nonsteroidal antiphlogistic analgestic agent of the present invention can only achieve a remarkable effect in comparison to any other random combination of drugs described in USP '302 or USP '874.

Favorable reconsideration and allowance is thus respectfully solicited.

Respectfully submitted,

Keiko YAMASAKI et al.

By: _____
Warren M. Cheek, Jr.
Registration No. 33,367
Attorney for Applicants

WMC/dlk
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
November 19, 2003